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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,137	LIU ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 23-43* is/are pending in the application.

4a) Of the above claim(s) *27-35* is/are withdrawn from consideration.

5)☒ Claim(s) *15, 23-26* is/are allowed.

6)☒ Claim(s) *1-14 and 36-43* is/are rejected.

7)☒ Claim(s) *4,7 and 40-43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/28/2005 has been entered.

2. Currently, claims 1-15, and 23-43 are pending in the instant application. Claims 27-35 have been withdrawn from consideration as being drawn to a nonelected invention. The amendments and arguments have been thoroughly reviewed but were found insufficient to place the instant application in condition for allowance. The following rejections are either newly applied or are reiterated and constitute the complete set being presently applied to the instant application. Response to arguments follow. The following office action is NON-FINAL.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The rejection of claim 15 under 35 USC 102(b) made at sections 11 and 12 of the previous office action are moot in view of the amendment to the claim.

Claim Rejections - 35 USC § 112

5. Claims 1-14 and 36-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER Rejection.

Claims 1, 8, and 36 have been amended to recite "and the nucleic acid specifically hybridizes under highly stringent conditions to SEQ ID NO: 5, 6, 7, or 8 or the complement thereof". The specification provides no support for hybridization of SEQ ID NOS 5-8 or the complement thereof "under highly stringent conditions". While the specification does provide certain hybridization conditions, the amendment to include "under highly stringent conditions" represents a broadening of the invention disclosed in the specification. The recitation of "highly stringent conditions" encompasses different conditions such as salt concentration and temperature, that have not been described in the specification. Thus, such amendment introduces new matter into the instantly pending claims.

6. Claims 8-14 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims reciting nucleic acid sets containing probes that comprise SEQ ID NOS 5-8 and are anywhere from 200 up to 1000 nucleotides long (claims 36-38), and nucleic acids obtained from amplification (claims 8-14) encompass mutants variants and homologs, as well as sequences from other species, that have not been taught or described by the specification. All of the claims referenced herein recite language that is sufficiently "open" such that the claims encompass unspecified sequences on either side of the recited SEQ ID NOS. Such nucleic acids therefore encompass a large genus of sequences that have not been disclosed or described by the specification. The single sequence of Accession number AP002562 does not represent a significant portion of the claimed genus of mutants, variants, homologs, and sequences from other species, encompassed by the broad claim recitation. For example, SEQ ID NO: 5 is found completely within Genbank accession number AE015280 which is directed to a strain of Shigella flexneri ([gi:24053029]: Shigella flexneri 2a str. 301 section 243 of 412 of the complete genome) submitted to Genbank in 2002, after the filing date of the instant application. The alignment is provided below:

Query (SEQ ID NO: 5): 1 aatacataacagaaacctgaaacacaa 27

Sbjct (Shigella flexneri 2a str.301) : 9155 aatacataacagaaacctgaaacacaa 9129

It is noted that SEQ ID NOS: 1-4 and 6-8 also are found completely within the genome for this strain of Shigella either in accession number AE015280 or AE 015281. This region of the shigella genome, however, is not completely complementary to the E. coli genome, therefore sequences containing unspecified sequences on either side of the indicated SEQ ID NOS or amplified by the recited primers (with regard to claims 8-14) encompass sequences from shigella flexneri, for example, that have not been taught or described in the specification. It is noted that

claims 8-14 recite "obtained from amplification of an E. coli nucleic acid", however this recitation is not limited to sequences from E. coli because it is well known in the art that E. coli can be, and is, transformed to expresses sequences from other species. Further, with regard to claims 8-14, it is also well known in the art that PCR can result in non specific amplification such that the claims broadly encompass amplification of mutants, variants, and homologs of the recited sequences, as well as sequences from other species.

It is noted that claim 8 has been amended to recite "and the nucleic acid specifically hybridizes under highly stringent conditions to SEQ ID NO: 5, 6, 7, or 8 or the complement thereof". Firstly, the specification provides no support for hybridization of SEQ ID NOS 5-8 or the complement thereof "under highly stringent conditions". While the specification does provide certain hybridization conditions, the amendment to include "under highly stringent conditions" represents a broadening of the invention disclosed in the specification. Thus, such amendment introduces new matter into the instantly pending claims. Additionally, the sequences of SEQ ID NOS: 5-8, as noted above, are not E. coli specific. These sequences are found within the genome of a strain of Shigella flexneri. This recitation, therefore, does not limit the genus of encompassed nucleic acids to those that are from naturally occurring E. coli as SEQ ID NOS 5-8 could hybridize to other species, for example, some strains of Shigella flexneri. This recitation encompasses homologs and variants of the open reading frames, ECs3458 and ECs3460 from any source, thus encompassing unknown, uncharacterized open reading frames. As stated previously, it is well known in the art that E. coli can be, and is, transformed to express sequences from other species, therefore, while a sequence amplified by two primers can include sequences from E. coli, it can also include sequences from other species.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the recited SEQ ID NOS, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25

USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Response to Arguments

7. The response dated 2/28/2005 traverses the rejection. The response asserts that the specification provides sufficient written description for amended claim 8 as evidenced by the USPTO's Written Description Guidelines, example 10. The response notes that in amended clam 2 of the example, a product by process claim, the claim is drawn to genomic DNA that must hybridize under a highly stringent condition to SEQ ID NO: 10 and that likewise, instant claim 8, also a product by process claim, is drawn to genomic DNA that must hybridize under a highly stringent condition to any of SEQ ID NO: 5-8 or the complement thereof. This argument has been thoroughly reviewed but was found unpersuasive. Firstly, as noted above, the specification provides no support for hybridization "under highly stringent conditions". Secondly, the conditions outlined in example 10: 6xSSC and 65 deg. C represent specific stringent conditions which are not disclosed in the instant specification. Further, example 10 of the guidelines sets forth that "The specification teaches that SEQ ID NO: 10 is an EST... a chromosome marker, and that any DNA which hybridizes under specified stringent conditions will be useful as a marker for detecting the presence of Burkitt's lymphoma". This is in contrast to the instant situation. The instant specification is directed to detecting E. coli, however the primers of SEQ ID NOS 1-4 and the probes of SEQ ID NOS 5-8, used to detect the amplicon, are not E. coli specific, but are also found within the genome of a strain of Shigella flexneri. Therefore in contrast to example 10 of the guidelines, which states "the art indicates that there is no substantial variation within the genus because of the stringency of hybridization conditions...", the sequences used in the instant product by process claims would yield products

with substantial variation, which have not been described by the instant specification. With regard to claims 36-38, the amendment of claim 36 to specify "highly stringent conditions" is not supported by the instantly filed specification. Further, as already noted above, SEQ ID NO: 5-8 are not E. coli specific. Additionally, as stated previously, it is well known in the art that E. coli can be, and is, transformed to express sequences from other species, therefore, while a sequence amplified by two primers can include sequences from E. coli, it can also include sequences from other species. For these reasons and the reasons already made of record, the rejection is maintained.

Indefinite

8. Claims 1-14 and 36-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite primers that contain a specific SEQ ID NO (SEQ ID NO: 1-4): but the claims also recite that the primer can be no shorter than 18 nucleotides in length. The term "containing" stipulates that the full sequence is present in the larger sequence, however SEQ ID NOS: 3 and 4 are each 24 nucleotides in length. Consequently, it is unclear how a sequence can "contain" either SEQ ID NO: 3 or 4 and be 18 nucleotides long. Further, the claims recite probes that contain a specific SEQ ID NO: (SEQ ID NOS: 5-8) but also recite that the probe is not shorter than 26 nucleotides. The term "containing" stipulates that the full sequence is present in the larger sequence, however SEQ ID NOS 5-7 are each 27 nucleotides in length.

Consequently, it is unclear how a sequence can "contain" either SEQ ID NO: 5, 6, or 7 and be 26 nucleotides long.

Response to Arguments

9. The response asserts that the amendments have overcome the rejection. However, the amendment has not made clear the metes and bounds of the claimed nucleic acid. In a telephone conversation with Jianming Hao on April 14, 2005, the examiner asked whether or not the claims were meant to encompass sequences comprising sequences from *within* the recited SEQ ID NOS. Applicant's representative indicated that they were not. Therefore, this rejection can be easily overcome by reciting for example: in claims 1 and 8, line 4, "wherein the first and second nucleic acids are up to 40 nucleotides in length"; in claims 3 and 10, "up to 30 nucleotides in length"; in claims 6 and 13, "up to 32 nucleotides in length"; and in claim 36, lines 1-2, "further comprising a third nucleic acid that is up to 1000 nucleotides in length".

10. Claims 37-43 lack sufficient antecedent basis for the recitation of "the nucleic acid of claim 36" because claim 36 is drawn to a set of nucleic acids. This rejection can be easily overcome by reciting "the set of nucleic acids of claim 36...".

Claim Rejections - 35 USC § 102

11. Claims 8-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession number Z70523 (1996).

The claims are drawn to a nucleic acid 'obtained' from amplification of an E. coli template with primers, however claim 8 does not make clear how the nucleic acid was

"obtained". This recitation has been broadly interpreted to encompass further steps, such as using the amplicon generated with the primers to "obtain" a nucleic acid through hybridization to genomic DNA. The sequence taught by Accession number Z70523 is an E. coli sequence that could be "obtained" by such method. The alignment of SEQ ID NOS 1-8 with Z70523 was provided with the office action mailed 4/1/2004.

Claim Rejections - 35 USC § 103

12. Claims 1-3, 5-6, 8-14 and 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Genbank Accession number AE005490 (first appeared in Genbank on 1/25/2001), Genbank Accession number AE000346 (December 1, 2000), Genbank accession number Z70523 (April 1996) and Genbank accession number D90887 (1997) in view of Hogan (US Patent 5,693,469), Hammond et al (Referred to as Hammond; US Patent 5,374,718), and Tijhie et al (Referred to as Tijhie; J. Microbiol. Meth. Vol. 18, pp 137-150, 1993) and further in view of Buck et al (Referred to as Buck: Biotechniques, vol. 27, pp 528-536, 1999).

Accession number AE005490 teaches a gene sequence from the E. coli genome at positions 1933-2670. The accession number specifically teaches that the encoded proteins for genes from positions 1933-3282 are 100% identical to E. coli K 12. Accession numbers AE000346 (December 1, 2000), Z70523 (April 1996) and D90887 also teach sequences from different strains of E. coli. The positions of each of SEQ ID NOS 1-8 within these accession numbers are provided. The accession numbers do not teach the sequences of SEQ ID NOS 1-8, Hammond teaches and exemplifies a method for picking probes for detection of a particular organism (in the case of Hammond it was for Chlamydia pneumoniae) that are species specific

(see abstract). Hammond teaches that probes are chosen upon alignment of different sequences of a particular region and that genus specific and species specific probes can be chosen based on the alignment of the sequences to target regions of similarity or differences (see col. 2, lines 49-60, and cols 4-8). Hogan teaches targeting sequences within the E. coli genome for detection of E. coli, and provides motivation for using nucleic acid based assays for detection of E. coli. Tijhie teaches a method of picking probes and primers for genus and species detection of Chlamydia. Tijhie teaches using computer assisted sequences analysis of known sequences to identify regions of similarity and differences to construct genus and species specific probes and primers (see abstract, fig. 1, pages 141-142). Buck teaches design strategies for choosing DNA primers. Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that *every single primer* worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, *every single control primer* functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers

functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect E. coli using nucleic acid based techniques as taught by Hogan. The ordinary artisan would have been motivated to do so given the teachings of Hogan that nucleic acid based methods could be used to detect E. coli. The ordinary artisan would have been motivated to construct probes and primers for the purpose of detecting E. coli because Tijhie exemplifies the successful detection of Chlamydia with a nucleic acid based detection method using primers and probes. Given that a large number of E. coli genomic sequences containing SEQ ID NOS 1-8 were known (see Accession numbers cited above) the ordinary artisan would have been motivated to use such sequences to detect E. coli in view of the large amount of teaching in the prior art as to how to pick probes and primers for the detection of a target organism when target sequences were known (see Hammond, Hogan, Tijhie, and Buck). The claims encompass a genus of nucleic acid sequences which the ordinary artisan would have been motivated to construct for the purpose of detecting E. coli. Given the known E. coli sequences and the large amount of direction given in the prior art, the ordinary artisan would have been motivated to construct a genus of primers and probes for detection of E. coli. The ordinary artisan would have been motivated to target this particular region of E coli because Accession Number AE005490 teaches that this region is conserved in E. coli. Further, given the teachings of Hammond and Tijhie, the ordinary artisan would also have observed that this region of E. coli was conserved upon aligning the available genomic sequences of E. coli and would have been motivated to target this conserved region for the purpose of constructing probes and

primers to detect E. coli. The genus of probes and primers that the skilled artisan would be motivated to construct given the teachings of the prior art are considered equivalent, for the purpose of detecting E. coli, to the genus of claimed probes and primers, absent secondary consideration. The claims encompass a fairly large genus and the ordinary artisan would have been motivated to generate a genus of equivalent probes and primers for the purpose of detecting E. coli, therefore the genus of sequences encompassed by the claims is obvious over the cited art. The state of the art was very high at the time the invention was filed with regard to picking primers and probes from already known sequences for the purpose of detecting the sequences as exemplified by the teachings of Buck, Hogan, Hammond, and Tijhie.

It is noted that the instant rejection has not been applied to claims 4, 7, 15, and 23-26. As exemplified by the specification, such specific sequences exhibited unexpected results in that they were capable of detecting E. coli and not a large number of other genus and species of bacteria, including certain strains of Shigella, which is known in the art to be closely related to E. coli. As such, claims directed to the scope of the unexpected results (that is the specific SEQ ID NOS) are allowable over the cited prior art. However, the remaining claims are broader in scope and are not directed to any specific sequence, but rather to a large genus of sequences. Further, addition of sequences on either side of SEQ ID NOS 1-8 would be expected to change the hybridization specificity of the resulting sequences as compared to those exemplified by the specification. Since an extremely large amount of prior art was available at the time the invention was filed with regard to picking probes and primers to already known sequences (the larger sequence from which the genus of sequences containing or comprising the recited SEQ ID NOS was known) for the purposes of detecting those sequences, the genus of sequences

encompassed by the claims is obvious over the teachings of the prior art. While picking the *specific* sequences of nucleic acid molecules consisting of any one of SEQ ID NOS 1-8 is not obvious as the prior art does not lead the ordinary artisan to pick the specific sequences consisting of SEQ ID NOS: 1-8, the claims are not directed to specific sequences but to a large genus of sequences which the prior art does provide motivation to construct for the purposes of detecting the large sequence from which the genus is derived. Further, the teachings of the prior art provide a reasonable expectation of success that such genus of sequences will be able to be used as probes and primers for detection of certain strains of E. coli.

Response to Arguments

13. The response dated 2/28/2005 traverses the rejection. The response as well as the declaration submitted under 35 C.F.R. 1.132, submitted 1/3/05 have been thoroughly reviewed but were found unpersuasive to overcome the rejection. The declaration by Dr. Bair states that a pair of PCR primers EC-23 and EC-24, that contain sequences selected from the E. coli genome (Genbank Accession No. AF319597), were synthesized based on the same strategy for selecting SEQ ID NOS 3 and 4. The declaration states that the primers were used to amplify the corresponding target genes from nucleic acid samples of E. coli subtypes H, I , A, T, and Non-pathogenic, as well as 6 negative control microbes and that SEQ ID NOS 3 and 4 resulted in amplification of a predicted 500 base pair product but that EC-23 and EC-24 failed to amplify a predicted 863 bp product. However, it is not clear from the declaration whether the samples of E. coli tested possessed the sequence of Accession number AF319598. This accession number teaches an E. coli intimin type epsilon (eaeA) gene. However, this gene is known in the art to exist in variant form and to be differently distributed among human and animal EPEC and EHEC

strains. For example, Mansfield et al (The Journal of Infectious Diseases, vol. 184, pages 803-807, 2001) teaches 99.2% identity of the eae epsilon gene from CTT as compared to human isolates (see abstract). Further, Oswald et al (Infection and Immunity, vol. 68, pages 64-71) teaches that the intimins are differently distributed among human and animal EPEC and EHEC strains (see page 67, col. 2). The declaration does not make clear which specific isolates of E. coli subtypes were used nor whether the sequence of Genbank Accession number AF319597 was present in the isolates tested. The "unexpected" property of SEQ ID NOS 3 and 4 in comparison to EC-23 and EC-24 is therefore unclear. The rejection under 35 USC 103 above sets forth that the primers and probes the ordinary artisan would be motivated to construct would be expected to amplify and detect the sequences for which they were designed to hybridize to due to 100% complementarity. Furthermore, even if the declaration were persuasive in showing unexpected results of SEQ ID NOS 3 and 4, the rejection set forth above does not reject the specific sequences of SEQ ID NOS 3 and 4. The claims rejected under 35 USC 103(a) above are broader in scope than the specific sequences of SEQ ID NO: 3 and 4. The MPEP is clear that for claims to be allowable under 35 USC 103 in view of unexpected results, the scope of the claims must be commensurate in scope with the unexpected results. See MPEP 716.02(d).:

716.02(d) [R-2] Unexpected Results Commensurate in Scope With Claimed Invention
Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support."

This section of the MPEP was set forth in the previous office action (see page 16).

At page 12, the response states "In response to the office action, Applicant's rebutted the rejection by presenting an unexpected property exhibited by the claimed nucleic acids. Nonetheless, the examiner maintained the rejection". This argument has been thoroughly

reviewed but was found unpersuasive. The specification does not, nor do any of the previous responses, provide unexpected results with regard to the broadly claimed primers and probes "containing" the sequences of SEQ ID NOS 1-8. The unexpected results set forth in the specification are limited to the specific sequences of SEQ ID NOS 1-8, not to sequences "containing" them. Nowhere does the specification (nor any of the previous responses or declaration) provide any unexpected results with a pair of primers containing any of SEQ ID NOS 1 or 3, and SEQ ID NOS 2 or 4, wherein the primers are up to 40, 32, or 30 nucleotides in length, or to a probe containing any of SEQ ID NOS 5-8, wherein the probe is up to 1000, 500, 200, or 50 nucleotides in length. Therefore, contrary to the responses assertion, Applicants have not presented any unexpected property with regard to these longer sequences which contain any of SEQ ID NOS 1-8.

The response seeks to put the examiner's reasoning in a different way, however the response's characterization at page 13, appears to misinterpret the rejection set forth above. Nowhere does the rejection state "claim 1 may cover PCR primers that do not hybridize to the complements of SEQ ID NOS: 1-4, and, therefore, would not generate E. coli specific products, ie: fail to exhibit the just mentioned unexpected results".

The rejection states : *It is noted that the instant rejection has not been applied to claims 4, 7, 15, and 23-26. As exemplified by the specification, such specific sequences exhibited unexpected results in that they were capable of detecting E. coli and not a large number of other genus and species of bacteria, including certain strains of Shigella, which is known in the art to be closely related to E. coli. As such, claims directed to the scope of the unexpected results (that is the specific SEQ ID NOS) are allowable over the cited prior art. However, the remaining*

claims are broader in scope and are not directed to any specific sequence, but rather to a large genus of sequences. Further, addition of sequences on either side of SEQ ID NOS 1-8 would be expected to change the hybridization specificity of the resulting sequences as compared to those exemplified by the specification. It is well known in the art that the length of a nucleic acid as well as its GC content will affect Tm and therefore the nucleic acid's specificity. The statement reiterated above was not directed to non E. coli sequences on either side of SEQ ID NOS 1-8, but rather to the fact that if sequences from the particular accession number that applicant's used to construct SEQ ID NOS 1-8 were included on either side of any of SEQ ID NOS 1-8 (that is the length of the primers and probes was increased with sequences respectively set forth in accession number AP002562), the subsequent change in length of the nucleic acids as well as the change in GC content would be expected to change the Tm of the nucleic acid and therefore it's specificity. The unexpected results with regard to the specific sequences of SEQ ID NOS 1-8 as set forth in the specification is that they exhibited unexpected specificity in that they were capable of distinguishing E. coli from a number of structurally similar microorganisms. For example, both Salmonella and Shigella are known in the art to possess nucleic acid sequences that have high nucleic acid identity to the E. coli genome. Lengthening the primers or probes of SEQ ID NOS 1-8 would be expected to change their Tm as well as their specificity. As evidenced in the sequence search for each of SEQ ID NOS 1-8, provided with the office action dated 4/1/2004, the sequences of SEQ ID NOS 1-8 are not E. coli specific. For these reasons and the reasons already made of record, the rejection is maintained.

Conclusion

14. Claims 4, 7, 15, 23-26, and 40-43 are free of the cited prior art. Claims 4, 7, and 40-43 are objected to for being dependent on rejected claims.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Jehanne Sitton

Jehanne Sitton
Primary Examiner
Art Unit 1634
5/12/05